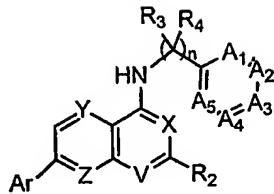


What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

(i) halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₁-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R₂), N(R₂)(C=O)_p, SO₂N(R₂) or N(R₂)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b;

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b; and

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

(i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

- (ii) taken together with R_4 attached to the same carbon atom to form an oxo group;
- (iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl;

Each R_4 is:

- (i) independently chosen from hydrogen, cyano and C_1 - C_4 alkyl; or
- (ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b ;

A_1 is N or CR_a , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_a ;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$; and
- (ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_8 alkoxycarbonyl, C_1 - C_8 alkylsulfonyl, mono- and di-(C_1 - C_8 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_8 alkyl)amino C_6 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino.

2. A compound or salt according to claim 1, wherein Ar is phenyl or pyridyl, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, $COOH$, aminocarbonyl, aminosulfonyl, cyano, nitro, C_1 - C_4 alkyl, C_1 - C_4 alkenyl, C_1 - C_4 alkynyl, halo C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo C_1 - C_4 alkoxy, C_1 - C_4 alkanoyl, C_1 - C_4 alkylsulfonyl, mono- and di-(C_1 - C_4 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_4 alkyl)amino C_6 - C_4 alkyl

3. A compound or salt according to claim 2, wherein Ar is phenyl or 2-pyridyl, each of which is substituted with from 1 to 3 substituents independently chosen from halogen, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy and halo C_1 - C_6 alkoxy.

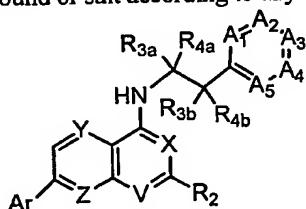
4. A compound or salt according to claim 3, wherein at least one substituent of Ar is located *ortho* to the point of attachment.

5. A compound or salt according to claim 4, wherein Ar is mono-substituted 2-pyridyl, wherein the substituent is halogen, trifluoromethyl or methyl.

6. A compound or salt according to any one of claims 1-5, wherein X and V are N.

7. A compound or salt according to claim 6, wherein Y is CH.

8. A compound or salt according to any one of claims 1-7, having the formula:



wherein:

R_{3a} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4a} to form an oxo group; or
- (iii) taken together with R_{4a} or R_{3b} to form a 3- to 5-membered carbocycle;

R_{3b} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4b} to form an oxo group;
- (iii) taken together with R_{4b} or R_{3a} to form a 3- to 5-membered carbocycle; or
- (iv) taken together with A₁ to form a fused 5- to 7-membered carbocycle;

R_{4a} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3a} to form an oxo group or a 3- to 5-membered carbocycle; and

R_{4b} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3b} to form an oxo group or a 3- to 5-membered carbocycle.

9. A compound or salt according to claim 8, wherein each of R_{3a}, R_{3b}, R_{4a} and R_{4b} is hydrogen.

10. A compound or salt according to claim 8, wherein R_{3a}, R_{4a} and R_{4b} are hydrogen, and R_{3b} is methyl or taken together with A₁ to form a fused cyclopentyl group.

11. A compound or salt according to claim 8, wherein either:

R_{3a} and R_{4a} are taken together to form an oxo group, and R_{3b} and R_{4b} are both hydrogen; or
 R_{3b} and R_{4b} are taken together to form an oxo group, and R_{3a} and R_{4a} are both hydrogen.

12. A compound or salt according to any one of claims 1-11, wherein:

A_1 is CR_a , or A_1 is taken together with a R_3 group to form a fused cyclopentyl or cyclohexyl group;

A_2 , A_3 and A_4 are independently CR_a ;

A_5 is N or CR_a ; and

R_a is independently chosen at each occurrence from hydrogen, halogen, cyano, C_1 - C_6 alkyl, $(C_3$ - C_6 cycloalkyl) C_0 - C_4 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, C_2 - C_4 alkyl ether, C_1 - C_6 alkanoyl, C_1 - C_6 alkylsulfonyl, aminosulfonyl, mono- and di- $(C_1$ - C_6 alkyl)aminosulfonyl, and mono- and di- $(C_1$ - C_6 alkyl)amino C_0 - C_4 alkyl.

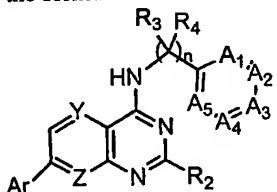
13. A compound or salt according to claim 12, wherein at least one R_a is not hydrogen.

14. A compound or salt according to claim 13, wherein R_a is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.

15. A compound or salt according to any one of claims 1-14, wherein R_2 is C_1 - C_6 alkyl, C_1 - C_6 alkenyl, C_2 - C_6 alkyl ether, mono- or di- $(C_1$ - C_6 alkyl)amino C_1 - C_6 alkyl, mono- or di- $(C_1$ - C_6 alkenyl)amino C_1 - C_6 alkyl, $(C_4$ - C_{10} carbocycle) C_1 - C_6 alkyl, (4- to 10-membered heterocycle) C_1 - C_6 alkyl, mono- or di- $(C_1$ - C_6 alkyl)amino C_2 - C_6 alkyl ether, $(C_4$ - C_{10} carbocycle) C_2 - C_6 alkyl ether or (4- to 10-membered heterocycle) C_2 - C_6 alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl.

16. A compound or salt according to claim 15, wherein R_2 is C_2 - C_6 alkyl ether, mono- or di- $(C_1$ - C_6 alkyl)amino C_1 - C_4 alkyl, mono- or di- $(C_1$ - C_6 alkenyl)amino C_1 - C_6 alkyl, or (4- to 10-membered heterocycloalkyl) C_1 - C_6 alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl.

17. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

Y and Z are each independently N or CR_1 ;

R_1 is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy and mono- and di- $(C_1$ - C_6 alkyl)amino;

R_2 is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula $-R_x-L-M-R_y$, wherein:

R_x is C_0-C_3 alkylene;

L is a single covalent bond, O, $(C=O)$, $(C=O)O$, $O(C=O)$, S, SO_2 , $(C=O)_pN(R_z)$,

$N(R_z)(C=O)_p$, $SO_2N(R_z)$ or $N(R_z)SO_2$, wherein p is 0 or 1;

M is a single covalent bond, C_1-C_8 alkyl, C_1-C_8 alkenyl or C_1-C_8 alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b ; and

R_y is:

(a) hydrogen;

(b) C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkoxy, $(C_1-C_8$ alkyl)amino C_0-C_8 alkyl, C_1-C_8 alkanoyl, C_2-C_8 alkanone, C_2-C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b ; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

R_z is:

(a) hydrogen;

(b) C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkanoyl, C_2-C_8 alkanone, C_2-C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b ; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

n is 1, 2 or 3;

Each R_3 is independently:

(i) chosen from hydrogen, cyano and C_1-C_4 alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

(ii) taken together with R_4 attached to the same carbon atom to form an oxo group;

(iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;

(iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or

(v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle;

wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1-C_4 alkyl and halo C_1-C_4 alkyl;

Each R_4 is independently:

(i) hydrogen, cyano or C_1-C_4 alkyl; or

(ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 1 to 3 substituents independently selected from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C₁-C₈alkyl, C₁-C₈alkenyl, C₁-C₈alkynyl, haloC₁-C₈alkyl, haloC₁-C₈alkoxy, C₁-C₈alkanoyl, C₃-C₈alkanone, C₁-C₈alkanoyloxy, C₁-C₈alkylthio, C₂-C₈alkyl ether, C₁-C₄alkoxycarbonyl, C₁-C₈alkylsulfonyl, mono- and di-(C₁-C₈alkyl)aminosulfonyl, and mono- and di-(C₁-C₈alkyl)aminoC₀-C₄alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, and mono- and di-(C₁-C₄alkyl)amino;

A₁ is N or CR₆, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR₆;

R₆ is independently chosen at each occurrence from hydrogen, R₅ and groups that are taken together with an adjacent R₆ to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R₅; and

R₅ is independently chosen at each occurrence from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C₁-C₈alkyl, C₁-C₈alkenyl, C₁-C₈alkynyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₁-C₈alkanoyl, C₃-C₈alkanone, C₁-C₈alkanoyloxy, C₁-C₈alkylthio, C₂-C₈alkyl ether, C₁-C₄alkoxycarbonyl, C₁-C₈alkylsulfonyl, mono- and di-(C₁-C₈alkyl)aminosulfonyl, and mono- and di-(C₁-C₈alkyl)aminoC₀-C₄alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, and mono- and di-(C₁-C₄alkyl)amino.

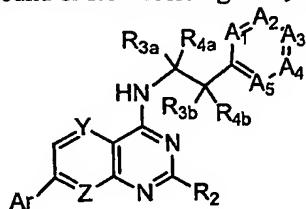
18. A compound or salt according to claim 17, wherein Ar is phenyl or pyridyl, each of which is substituted with from 1 to 3 substituents independently chosen from hydroxy, halogen, amino, COOH, aminocarbonyl, aminosulfonyl, cyano, nitro, C₁-C₄alkyl, C₁-C₄alkenyl, C₁-C₄alkynyl, haloC₁-C₄alkyl, haloC₁-C₄alkoxy, C₁-C₄alkanoyl, C₁-C₄alkylsulfonyl, mono- and di-(C₁-C₄alkyl)aminosulfonyl, and mono- and di-(C₁-C₄alkyl)aminoC₀-C₄alkyl.

19. A compound or salt according to claim 18, wherein at least one substituent of Ar is located *ortho* to the point of attachment.

20. A compound or salt according to claim 19, wherein Ar is mono-substituted 2-pyridyl, wherein the substituent is halogen, trifluoromethyl or methyl.

21. A compound or salt according to any one of claims 17-20, wherein Y is CH.

22. A compound or salt according to any one of claims 17-21, having the formula:



wherein:

R_{3a} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4a} to form an oxo group; or
- (iii) taken together with R_{4a} or R_{3b} to form a 3- to 5-membered carbocycle;

R_{3b} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4b} to form an oxo group;
- (iii) taken together with R_{4b} or R_{3a} to form a 3- to 5-membered carbocycle; or
- (iv) taken together with A₁ to form a fused 5- to 7-membered carbocycle;

R_{4a} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3a} to form an oxo group or a 3- to 5-membered carbocycle; and

R_{4b} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3b} to form an oxo group or a 3- to 5-membered carbocycle.

23. A compound or salt according to claim 22, wherein each of R_{3a}, R_{3b}, R_{4a} and R_{4b} is hydrogen.

24. A compound or salt according to claim 22, wherein R_{3a}, R_{4a} and R_{4b} are hydrogen, and R_{3b} is methyl or taken together with A₁ to form a fused cyclopentyl group.

25. A compound or salt according to claim 22, wherein either:

R_{3a} and R_{4a} are taken together to form an oxo group, and R_{3b} and R_{4b} are both hydrogen; or
R_{3b} and R_{4b} are taken together to form an oxo group, and R_{3a} and R_{4a} are both hydrogen.

26. A compound or salt according to any one of claims 17-25, wherein:

A₁ is CR_n, or A₁ is taken together with a R₃ group to form a fused cyclopentyl or cyclohexyl group;

A₂, A₃ and A₄ are independently CR_n;

A₅ is N or CR_n; and

R_n is independently chosen at each occurrence from hydrogen, halogen, cyano, C₁-C₆alkyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy, C₂-C₄alkyl ether, C₁-C₄alkanoyl, C₁-C₆alkylsulfonyl, and mono- and di-(C₁-C₆alkyl)aminoC₀-C₄alkyl.

27. A compound or salt according to claim 26, wherein at least one R_a is not hydrogen.

28. A compound or salt according to claim 27, wherein R_a is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.

29. A compound or salt according to any one of claims 17-28, wherein R_2 is:

(i) halogen, nitro or cyano; or

(ii) a group of the formula $-R_x-L-M-R_y$, wherein:

R_x is C_1-C_3 alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), (C=O)_pN(R_2) or N(R_2)(C=O)_p,

wherein p is 0 or 1;

M is a single covalent bond or C_1-C_8 alkylene that substituted with from 0 to 4 substituents independently selected from R_b ;

R_y is:

(a) hydrogen;

(b) C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkoxy, (C_1-C_8 alkyl)amino C_0-C_8 alkyl, C_1-C_8 alkanoyl, C_2-C_8 alkanone, C_2-C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from R_b ; or

(c) taken together with R_z to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from R_b ; and

R_z is:

(a) hydrogen;

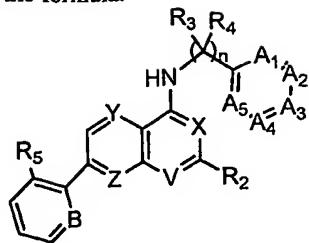
(b) C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from R_b ; or

(c) taken together with R_y to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from R_b .

30. A compound or salt according to any one of claims 17-28, wherein R_2 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_2-C_6 alkyl ether, mono- or di- $(C_1-C_6$ alkyl)amino C_1-C_6 alkyl, mono- or di- $(C_1-C_6$ alkenyl)amino C_1-C_6 alkyl, $(C_4-C_{10}$ carbocycle) C_1-C_6 alkyl, (4- to 10-membered heterocycle) C_1-C_6 alkyl, mono- or di- $(C_1-C_6$ alkyl)amino C_2-C_6 alkyl ether, $(C_4-C_{10}$ carbocycle) C_2-C_6 alkyl ether, or (4- to 10-membered heterocycle) C_2-C_6 alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C_1-C_4 alkyl and halo C_1-C_4 alkyl.

31. A compound or salt according to claim 30, wherein R_2 is C_2-C_6 alkyl ether, mono- or di- $(C_1-C_6$ alkyl)amino C_1-C_4 alkyl, mono- or di- $(C_1-C_6$ alkenyl)amino C_1-C_6 alkyl, or (4- to 10-membered heterocycloalkyl) C_1-C_4 alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C_1-C_4 alkyl and halo C_1-C_4 alkyl.

32. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

Y and Z are each independently N or CR₁;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

B is CH or N;

R₅ is hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro, C₁-C₄alkyl, C₁-C₄alkenyl, C₁-C₄alkynyl, haloC₁-C₄alkyl, C₁-C₄alkoxy, haloC₁-C₄alkoxy, C₁-C₄alkanoyl, C₁-C₄alkylsulfonyl, mono- and di-(C₁-C₄alkyl)aminosulfonyl, and mono- and di-(C₁-C₄alkyl)aminoC₀-C₄alkyl;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

n is 1, 2 or 3;

Each R_3 is independently:

- (i) chosen from hydrogen, cyano and C_1 - C_4 alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R_4 attached to the same carbon atom to form an oxo group;
- (iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl;

Each R_4 is independently:

- (i) hydrogen, cyano or C_1 - C_4 alkyl; or
- (ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

A_1 is N or CR_a , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_a ;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

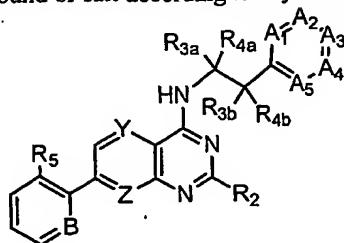
- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$; and
- (ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_4 alkoxycarbonyl, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_0 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino.

33. A compound or salt according to claim 32, wherein R_5 is halogen, trifluoromethyl or methyl.

34. A compound or salt according to claim 32 or claim 33, wherein X and V are N.

35. A compound or salt according to claim 34, wherein Y is CH.

36. A compound or salt according to any one of claims 32-35, having the formula:



wherein:

R_{3a} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4a} to form an oxo group; or
- (iii) taken together with R_{4a} or R_{3b} to form a 3- to 5-membered carbocycle;

R_{3b} is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R_{4b} to form an oxo group;
- (iii) taken together with R_{4b} or R_{3a} to form a 3- to 5-membered carbocycle; or
- (iv) taken together with A₁ to form a fused 5- to 7-membered carbocycle;

R_{4a} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3a} to form an oxo group or a 3- to 5-membered carbocycle; and

R_{4b} is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R_{3b} to form an oxo group or a 3- to 5-membered carbocycle.

37. A compound or salt according to claim 36, wherein each of R_{3a}, R_{3b}, R_{4a} and R_{4b} is hydrogen.

38. A compound or salt according to claim 36, wherein R_{3a}, R_{4a} and R_{4b} are hydrogen, and R_{3b} is methyl or taken together with A₁ to form a fused cyclopentyl group.

39. A compound or salt according to claim 36, wherein either:

R_{3a} and R_{4a} are taken together to form an oxo group, and R_{3b} and R_{4b} are both hydrogen; or
 R_{3b} and R_{4b} are taken together to form an oxo group, and R_{3a} and R_{4a} are both hydrogen.

40. A compound or salt according to any one of claims 32-39, wherein:

A₁ is CR_{4a}, or A₁ is taken together with a R₃ group to form a fused cyclopentyl or cyclohexyl group;

A₂, A₃ and A₄ are independently CR_{4a};

A₅ is N or CR_{4a}; and

R_a is independently chosen at each occurrence from hydrogen, halogen, cyano, C_1 - C_6 alkyl, (C_3 - C_8 cycloalkyl) C_0 - C_6 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy, C_2 - C_4 alkyl ether, C_1 - C_4 alkanoyl, C_1 - C_6 alkylsulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_0 - C_4 alkyl.

41. A compound or salt according to claim 40, wherein at least one R_a is not hydrogen.

42. A compound or salt according to claim 41, wherein R_a is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.

43. A compound or salt according to any one of claims 32-42, wherein R_2 is:

(i) halogen, nitro or cyano; or

(ii) a group of the formula $-R_x-L-M-R_y$, wherein:

R_x is C_1 - C_3 alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), (C=O)_pN(R_z) or N(R_z)(C=O)_p,

wherein p is 0 or 1;

M is a single covalent bond or C_1 - C_8 alkylene that substituted with from 0 to 4 substituents independently selected from R_b ;

R_y is:

(a) hydrogen;

(b) C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_1 - C_8 alkoxy, (C_1 - C_8 alkyl)amino C_0 - C_8 alkyl, C_1 - C_8 alkanoyl, C_2 - C_8 alkanone, C_2 - C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from R_b ; or

(c) taken together with R_z to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from R_b ; and

R_z is:

(a) hydrogen;

(b) C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from R_b ; or

(c) taken together with R_y to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from R_b .

44. A compound or salt according to any one of claims 32-42, wherein R_2 is hydrogen, C_1 - C_6 alkyl, C_1 - C_6 alkenyl, C_2 - C_6 alkyl ether, mono- or di-(C_1 - C_6 alkyl)amino C_1 - C_6 alkyl, mono- or di-(C_1 - C_6 alkenyl)amino C_1 - C_6 alkyl, (C_4 - C_{10} carbocycle) C_1 - C_6 alkyl, (4- to 10-membered heterocycle) C_1 - C_6 alkyl, mono- or di-(C_1 - C_6 alkyl)amino C_2 - C_6 alkyl ether, (C_4 - C_{10} carbocycle) C_2 - C_6 alkyl ether, or (4- to 10-membered heterocycle) C_2 - C_6 alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl.

45. A compound or salt according to claim 44, wherein R₂ is C₂-C₆alkyl ether, mono- or di-(C₁-C₆alkyl)aminoC₁-C₄alkyl, mono- or di-(C₁-C₆alkenyl)aminoC₁-C₆alkyl, or (4- to 10-membered heterocycloalkyl)C₁-C₄alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C₁-C₄alkyl and haloC₁-C₄alkyl.

46. A compound or salt according to any one of claims 1-45, wherein the compound exhibits no detectable agonist activity an *in vitro* assay of capsaicin receptor agonism.

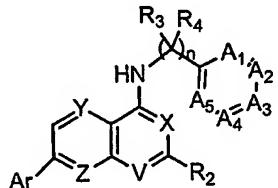
47. A compound or salt according to any one of claims 1-45, wherein the compound has an IC₅₀ value of 100 nanomolar or less in a capsaicin receptor calcium mobilization assay.

48. A compound or salt according to any one of claims 1-45, wherein the compound has an IC₅₀ value of 10 nanomolar or less in a capsaicin receptor calcium mobilization assay.

49. A pharmaceutical composition, comprising at least one compound or salt according to any one of claims 1-45, in combination with a physiologically acceptable carrier or excipient.

50. A pharmaceutical composition according to claim 49 wherein the composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

51. A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;
 R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

- (a) hydrogen;
- (b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or
- (c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

- (a) hydrogen;
- (b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or
- (c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

- (i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R₄ attached to the same carbon atom to form an oxo group;
- (iii) taken together with R₄ attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R₃ group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A₁ to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C₁-C₄alkyl and haloC₁-C₄alkyl;

Each R₄ is independently:

- (i) hydrogen, cyano or C₁-C₄alkyl; or
- (ii) taken together with R₃ attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b;

A₁ is N or CR_a, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR_a;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$;
and
- (ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_4 alkoxycarbonyl, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_6 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino;

and thereby reducing calcium conductance of the capsaicin receptor.

52. A method according to claim 51, wherein the compound is a compound according to claim any one of claims 1-45.

53. A method according to claim 51, wherein the cell is contacted *in vivo* in an animal.

54. A method according to claim 53, wherein the cell is a neuronal cell.

55. A method according to claim 53, wherein the cell is a urothelial cell.

56. A method according to claim 55, wherein during contact the compound is present within a body fluid of the animal.

57. A method according to claim 56, wherein the compound is present in the blood of the animal at a concentration of 1 micromolar or less.

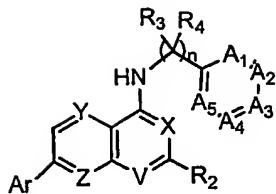
58. A method according to claim 57, wherein the compound is present in the blood of the animal at a concentration of 500 nanomolar or less.

59. A method according to claim 57, wherein the compound is present in the blood of the animal at a concentration of 100 nanomolar or less.

60. A method according to claim 53, wherein the animal is a human.

61. A method according to claim 53, wherein the compound is administered orally.

62. A method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*, the method comprising contacting capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

(i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

(ii) taken together with R₄ attached to the same carbon atom to form an oxo group;

(iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;

(iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or

(v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle;

wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl;

Each R_4 is independently:

(i) hydrogen, cyano or C_1 - C_4 alkyl; or

(ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b ;

A_1 is N or CR_a , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_a ;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

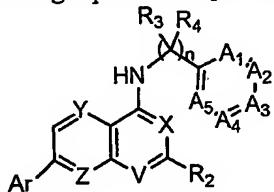
(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$; and

(ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_8 alkoxycarbonyl, C_1 - C_8 alkylsulfonyl, mono- and di-(C_1 - C_8 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_8 alkyl)amino C_0 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino;

under conditions and in an amount sufficient to detectably inhibit vanilloid ligand binding to capsaicin receptor.

63. A method according to claim 62, wherein the compound is a compound according to claim any one of claims 1-45.

64. A method for inhibiting binding of vanilloid ligand to capsaicin receptor in a patient, comprising contacting cells expressing capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

(i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

(ii) taken together with R₄ attached to the same carbon atom to form an oxo group;
 (iii) taken together with R₄ attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
 (iv) taken together with a second R₃ group to form a 3- to 7-membered carbocycle; or
 (v) taken together with A₁ to form a fused 5- to 7-membered carbocycle or heterocycle;
 wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C₁-C₄alkyl and haloC₁-C₄alkyl;

Each R₄ is independently:

- (i) hydrogen, cyano or C₁-C₄alkyl; or
- (ii) taken together with R₃ attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b;

A₁ is N or CR_a, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR_a;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b; and

R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH;
 and
- (ii) C₁-C₈alkyl, C₁-C₈alkenyl, C₁-C₈alkynyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₁-C₈alkanoyl, C₃-C₈alkanone, C₁-C₈alkanoyloxy, C₁-C₈alkylthio, C₂-C₈alkyl ether, C₁-C₄alkoxycarbonyl, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)aminosulfonyl, and mono- and di-(C₁-C₆alkyl)aminoC₆-C₄alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, and mono- and di-(C₁-C₄alkyl)amino;

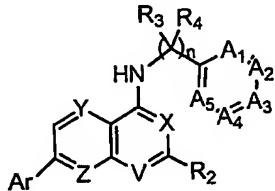
and thereby inhibiting binding of vanilloid ligand to the capsaicin receptor in the patient.

65. A method according to claim 64, wherein the compound is a compound according to claim any one of claims 1-45.

66. A method according to claim 64, wherein the patient is a human.

67. A method according to claim 64, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

68. A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

- (i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R₄ attached to the same carbon atom to form an oxo group;
- (iii) taken together with R₄ attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R₃ group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A₁ to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C₁-C₄alkyl and haloC₁-C₄alkyl;

Each R₄ is independently:

- (i) hydrogen, cyano or C₁-C₄alkyl; or
- (ii) taken together with R₃ attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b;

A₁ is N or CR_a, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR_a;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b; and

R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C₁-C₈alkyl, C₁-C₈alkenyl, C₁-C₈alkynyl, haloC₁-C₈alkyl, C₁-C₈alkoxy, haloC₁-C₈alkoxy, C₁-C₈alkanoyl, C₃-C₈alkanone, C₁-C₈alkanoyloxy, C₁-C₈alkylthio, C₂-C₈alkyl ether, C₁-C₄alkoxycarbonyl, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)aminosulfonyl, and mono- and di-(C₁-C₆alkyl)aminoC₀-C₄alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, and mono- and di-(C₁-C₄alkyl)amino;

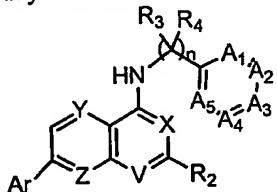
and thereby alleviating the condition in the patient.

69. A method according to claim 68, wherein the compound is a compound according to claim any one of claims 1-45.

70. A method according to claim 68, wherein the patient is suffering from (i) exposure to capsaicin, (ii) burn or irritation due to exposure to heat, (iii) burns or irritation due to exposure to light, (iv) burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants or pepper spray, or (v) burn or irritation due to exposure to acid.

71. A method according to claim 68, wherein the condition is asthma or chronic obstructive pulmonary disease.

72. A method for treating pain in a patient, comprising administering to a patient suffering from pain a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;

R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R_3 is independently:

- (i) chosen from hydrogen, cyano and C_1 - C_4 alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R_4 attached to the same carbon atom to form an oxo group;
- (iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl;

Each R_4 is independently:

- (i) hydrogen, cyano or C_1 - C_4 alkyl; or
- (ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b ;

A_1 is N or CR_a , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_a ;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$; and
- (ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_4 alkoxycarbonyl, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_6 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino;

and thereby alleviating pain in the patient.

73. A method according to claim 72, wherein the compound is a compound according to claim any one of claims 1-45.

74. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

75. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 500 nanomolar or less.

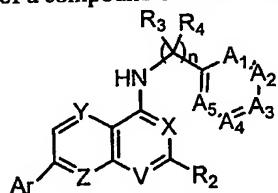
76. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 100 nanomolar or less.

77. A method according to claim 72, wherein the patient is suffering from neuropathic pain.

78. A method according to claim 72, wherein the pain is associated with a condition selected from: postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, toothache, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, neuritis, neuronitis, neuralgia, AIDS-related neuropathy, MS-related neuropathy, spinal cord injury-related pain, surgery-related pain, musculoskeletal pain, back pain, headache, migraine, angina, labor, hemorrhoids, dyspepsia, Charcot's pains, intestinal gas, menstruation, cancer, venom exposure, irritable bowel syndrome, inflammatory bowel disease and trauma.

79. A method according to claim 72, wherein the patient is a human.

80. A method for treating itch in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N;
 R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C₁-C₆alkyl, haloC₁-C₆alkyl, C₁-C₆alkoxy, haloC₁-C₆alkoxy and mono- and di-(C₁-C₆alkyl)amino;

R₂ is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C₀-C₃alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R_z), N(R_z)(C=O)_p, SO₂N(R_z) or N(R_z)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C₁-C₈alkyl, C₁-C₈alkenyl or C₁-C₈alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

- (a) hydrogen;
- (b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkoxy, (C₁-C₈alkyl)aminoC₀-C₈alkyl, C₁-C₈alkanoyl, C₂-C₈alcanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or
- (c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

- (a) hydrogen;
- (b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alcanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or
- (c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

- (i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R₄ attached to the same carbon atom to form an oxo group;
- (iii) taken together with R₄ attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R₃ group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A₁ to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C₁-C₄alkyl and haloC₁-C₄alkyl;

Each R₄ is independently:

- (i) hydrogen, cyano or C₁-C₄alkyl; or
- (ii) taken together with R₃ attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b;

A₁ is N or CR_a, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR_a;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

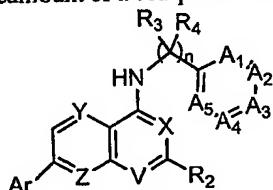
R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$;
- and
- (ii) C_1-C_8 alkyl, C_1-C_8 alkenyl, C_1-C_8 alkynyl, halo C_1-C_8 alkyl, C_1-C_8 alkoxy, halo C_1-C_8 alkoxy, C_1-C_8 alkanoyl, C_3-C_8 alkanone, C_1-C_8 alkanoyloxy, C_1-C_8 alkylthio, C_2-C_8 alkyl ether, C_1-C_4 alkoxycarbonyl, C_1-C_6 alkylsulfonyl, mono- and di-(C_1-C_6 alkyl)aminosulfonyl, and mono- and di-(C_1-C_6 alkyl)amino C_0-C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, hydroxy C_1-C_4 alkyl, halo C_1-C_4 alkyl, and mono- and di-(C_1-C_4 alkyl)amino;

and thereby alleviating itch in the patient.

81. A method according to claim 80, wherein the compound is a compound according to claim any one of claims 1-45.

82. A method for treating cough or hiccup in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V , X , Y and Z are each independently N or CR_1 , such that at least one of V and X is N ;
 R_1 is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C_1-C_6 alkyl, halo C_1-C_6 alkyl, C_1-C_6 alkoxy, halo C_1-C_6 alkoxy and mono- and di-(C_1-C_6 alkyl)amino;

R_2 is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula $-R_x-L-M-R_y$, wherein:

R_x is C_0-C_3 alkylene;
 L is a single covalent bond, O , $(C=O)$, $(C=O)O$, $O(C=O)$, S , SO_2 , $(C=O)_pN(R_z)$, $N(R_z)(C=O)_p$, $SO_2N(R_z)$ or $N(R_z)SO_2$, wherein p is 0 or 1;

M is a single covalent bond, C_1-C_8 alkyl, C_1-C_8 alkenyl or C_1-C_8 alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b ; and

R_y is:

- (a) hydrogen;

- (b) $C_1\text{-}C_8\text{alkyl}$, $C_2\text{-}C_8\text{alkenyl}$, $C_2\text{-}C_8\text{alkynyl}$, $C_1\text{-}C_8\text{alkoxy}$, $(C_1\text{-}C_8\text{alkyl})\text{amino}C_0\text{-}C_8\text{alkyl}$, $C_1\text{-}C_8\text{alkanoyl}$, $C_2\text{-}C_8\text{alkanone}$, $C_2\text{-}C_8\text{alkyl}$ ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b ; or
- (c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

R_z is:

- (a) hydrogen;
- (b) $C_1\text{-}C_8\text{alkyl}$, $C_2\text{-}C_8\text{alkenyl}$, $C_2\text{-}C_8\text{alkynyl}$, $C_1\text{-}C_8\text{alkanoyl}$, $C_2\text{-}C_8\text{alkanone}$, $C_2\text{-}C_8\text{alkyl}$ ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b ; or
- (c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

n is 1, 2 or 3;

Each R_3 is independently:

- (i) chosen from hydrogen, cyano and $C_1\text{-}C_4\text{alkyl}$ that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R_4 attached to the same carbon atom to form an oxo group;
- (iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, $C_1\text{-}C_4\text{alkyl}$ and $\text{halo}C_1\text{-}C_4\text{alkyl}$;

Each R_4 is independently:

- (i) hydrogen, cyano or $C_1\text{-}C_4\text{alkyl}$; or
- (ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b ;

A_1 is N or CR_a , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_a ;

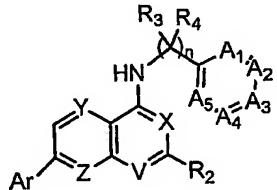
R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-\text{COOH}$;
 and
 (ii) $\text{C}_1\text{-C}_8\text{alkyl}$, $\text{C}_1\text{-C}_8\text{alkenyl}$, $\text{C}_1\text{-C}_8\text{alkynyl}$, $\text{haloC}_1\text{-C}_8\text{alkyl}$, $\text{C}_1\text{-C}_8\text{alkoxy}$, $\text{haloC}_1\text{-C}_8\text{alkoxy}$, $\text{C}_1\text{-C}_8\text{alkanoyl}$, $\text{C}_3\text{-C}_8\text{alkanone}$, $\text{C}_1\text{-C}_8\text{alkanoyloxy}$, $\text{C}_1\text{-C}_8\text{alkylthio}$, $\text{C}_2\text{-C}_8\text{alkyl}$ ether, $\text{C}_1\text{-C}_4\text{alkoxycarbonyl}$, $\text{C}_1\text{-C}_6\text{alkylsulfonyl}$, mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})\text{aminosulfonyl}$, and mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})\text{aminoC}_0\text{-C}_4\text{alkyl}$; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, $\text{C}_1\text{-C}_4\text{alkyl}$, $\text{C}_1\text{-C}_4\text{alkoxy}$, hydroxy $\text{C}_1\text{-C}_4\text{alkyl}$, $\text{haloC}_1\text{-C}_4\text{alkyl}$, and mono- and di- $(\text{C}_1\text{-C}_4\text{alkyl})\text{amino}$;
 and thereby alleviating cough or hiccup in the patient.

83. A method according to claim 82, wherein the compound is a compound according to claim any one of claims 1-45.

84. A method for treating urinary incontinence or overactive bladder in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V , X , Y and Z are each independently N or CR_1 , such that at least one of V and X is N ;
 R_1 is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{haloC}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{alkoxy}$, $\text{haloC}_1\text{-C}_6\text{alkoxy}$ and mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})\text{amino}$;

R_2 is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula $-\text{R}_x\text{-L-M-R}_y$, wherein:

R_x is $\text{C}_0\text{-C}_3\text{alkylene}$;

L is a single covalent bond, O , $(\text{C}=\text{O})$, $(\text{C}=\text{O})\text{O}$, $\text{O}(\text{C}=\text{O})$, S , SO_2 , $(\text{C}=\text{O})_p\text{N}(\text{R}_z)$, $\text{N}(\text{R}_z)(\text{C}=\text{O})_p$, $\text{SO}_2\text{N}(\text{R}_z)$ or $\text{N}(\text{R}_z)\text{SO}_2$, wherein p is 0 or 1;

M is a single covalent bond, $\text{C}_1\text{-C}_8\text{alkyl}$, $\text{C}_1\text{-C}_8\text{alkenyl}$ or $\text{C}_1\text{-C}_8\text{alkynyl}$, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b ; and

R_y is:

(a) hydrogen;

(b) $\text{C}_1\text{-C}_8\text{alkyl}$, $\text{C}_2\text{-C}_8\text{alkenyl}$, $\text{C}_2\text{-C}_8\text{alkynyl}$, $\text{C}_1\text{-C}_8\text{alkoxy}$, $(\text{C}_1\text{-C}_8\text{alkyl})\text{aminoC}_0\text{-C}_8\text{alkyl}$, $\text{C}_1\text{-C}_8\text{alkanoyl}$, $\text{C}_2\text{-C}_8\text{alkanone}$, $\text{C}_2\text{-C}_8\text{alkyl}$ ether, or a 4- to 10-membered

carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

(a) hydrogen;

(b) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, C₁-C₈alkanoyl, C₂-C₈alkanone, C₂-C₈alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

n is 1, 2 or 3;

Each R₃ is independently:

(i) chosen from hydrogen, cyano and C₁-C₄alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

(ii) taken together with R₄ attached to the same carbon atom to form an oxo group;

(iii) taken together with R₄ attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;

(iv) taken together with a second R₃ group to form a 3- to 7-membered carbocycle; or

(v) taken together with A₁ to form a fused 5- to 7-membered carbocycle or heterocycle;

wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C₁-C₄alkyl and haloC₁-C₄alkyl;

Each R₄ is independently:

(i) hydrogen, cyano or C₁-C₄alkyl; or

(ii) taken together with R₃ attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b;

A₁ is N or CR_a, or A₁ is taken together with a R₃ group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A₂, A₃, A₄ and A₅ are independently N or CR_a;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b; and

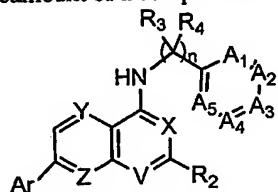
R_b is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH;
and

(ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_4 alkoxycarbonyl, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_0 - C_4 alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy, hydroxy C_1 - C_4 alkyl, halo C_1 - C_4 alkyl, and mono- and di-(C_1 - C_4 alkyl)amino; and thereby alleviating urinary incontinence or overactive bladder in the patient.

85. A method according to claim 84, wherein the compound is a compound according to claim any one of claims 1-45.

86. A method promoting weight loss in an obese patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR₁, such that at least one of V and X is N; R₁ is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C_1 - C_6 alkyl, halo C_1 - C_6 alkyl, C_1 - C_6 alkoxy, halo C_1 - C_6 alkoxy and mono- and di-(C_1 - C_6 alkyl)amino;

R₂ is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R_x-L-M-R_y, wherein:

R_x is C_0 - C_3 alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO₂, (C=O)_pN(R₂), N(R₂)(C=O)_p, SO₂N(R₂) or N(R₂)SO₂, wherein p is 0 or 1;

M is a single covalent bond, C_1 - C_8 alkyl, C_1 - C_8 alkenyl or C_1 - C_8 alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R_b; and

R_y is:

(a) hydrogen;

(b) C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_1 - C_8 alkoxy, (C₁-C₈alkyl)amino C_0 - C_8 alkyl, C_1 - C_8 alkanoyl, C_2 - C_8 alkanone, C_2 - C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b; or

(c) taken together with R_x or R_z to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b;

R_z is:

- (a) hydrogen;
- (b) C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, C_1 - C_8 alkanoyl, C_2 - C_8 alkanone, C_2 - C_8 alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R_b ; or
- (c) taken together with R_x or R_y to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R_b ;

n is 1, 2 or 3;

Each R_3 is independently:

- (i) chosen from hydrogen, cyano and C_1 - C_4 alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R_4 attached to the same carbon atom to form an oxo group;
- (iii) taken together with R_4 attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R_3 group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A_1 to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C_1 - C_4 alkyl and halo C_1 - C_4 alkyl;

Each R_4 is independently:

- (i) hydrogen, cyano or C_1 - C_4 alkyl; or
- (ii) taken together with R_3 attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R_b ;

A_1 is N or CR_4 , or A_1 is taken together with a R_3 group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A_2 , A_3 , A_4 and A_5 are independently N or CR_4 ;

R_a is independently chosen at each occurrence from hydrogen, R_b and groups that are taken together with an adjacent R_a to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R_b ; and

R_b is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and $-COOH$; and
- (ii) C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_1 - C_8 alkynyl, halo C_1 - C_8 alkyl, C_1 - C_8 alkoxy, halo C_1 - C_8 alkoxy, C_1 - C_8 alkanoyl, C_3 - C_8 alkanone, C_1 - C_8 alkanoyloxy, C_1 - C_8 alkylthio, C_2 - C_8 alkyl ether, C_1 - C_4 alkoxycarbonyl, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)aminosulfonyl, and mono- and di-(C_1 - C_6 alkyl)amino C_0 - C_4 alkyl; each of which is substituted with from 0 to 3

substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, hydroxyC₁-C₄alkyl, haloC₁-C₄alkyl, and mono- and di-(C₁-C₄alkyl)amino; and thereby promoting weight loss in the patient.

87. A method according to claim 86, wherein the compound is a compound according to claim any one of claims 1-45.

88. A compound or salt according to any one of claims 1-45, wherein the compound or salt is radiolabeled.

89. A method for determining the presence or absence of capsaicin receptor in a sample, comprising the steps of:

- (a) contacting a sample with a compound or salt according to any one of claims 1-45, under conditions that permit binding of the compound to capsaicin receptor; and
- (b) detecting a level of the compound bound to capsaicin receptor, and therefrom determining the presence or absence of capsaicin receptor in the sample.

90. A method according to claim 89, wherein the compound is a radiolabeled compound according to claim 88, and wherein the step of detection comprises the steps of:

- (i) separating unbound compound from bound compound; and
- (ii) detecting the presence or absence of bound compound in the sample.

91. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat pain.

92. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat cough or hiccup.

93. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat obesity.

94. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat urinary incontinence or overactive bladder.

95. The use of a compound or salt according to any one of claims 1-45 for the manufacture of a medicament for the treatment of a condition responsive to capsaicin receptor modulation.

96. A use according to claim 95, wherein the condition is pain, asthma, chronic obstructive pulmonary disease, cough, hiccup, obesity, urinary incontinence, overactive bladder, exposure to capsaicin, burn or irritation due to exposure to heat, burn or irritation due to exposure to light, burn, bronchoconstriction or irritation due to exposure to tear gas, infectious agent, air pollutants or pepper spray, or burn or irritation due to exposure to acid.